REMARKS

Claims 13-36, 38, and 42-43 are pending in the application. Claims 13, 14, 16-18, 20-22, 24-29, 35, 36, and 42 are amended. Support for the amendments can be found throughout the specification. For example, support for the term "symptoms" added to claims 13, 35, 36, and 42 can be found, *e.g.*, at page 2, lines 22-28, and at page 4, lines 8-10. Claim 36 has been amended to say "asthma triggering event," consistent with, *e.g.*, claims 33 and 34. This is suggested, *e.g.*, at page 3, lines 7-9. The remaining amendments merely clarify the intended scope of the claims. No new matter has been added by the amendment.

35 U.S.C. § 112, first paragraph

The Examiner maintained the rejection of claims 13, 35, 36, and 42 for lack of enablement. The Examiner stated that "the specification, while being enabling for the treatment of an acute episode of asthma, does not reasonably provide enablement for the 'prevention of an acute episode of asthma.'" *See* Office Action at page 3. The Examiner stated that Applicant's previous arguments were "not persuasive because the guidance provided by the specification is directed toward the treatment rather than the prevention of an acute episode of asthma and all working examples provided by the specification are directed toward the treatment rather than prevention of an acute episode of asthma..." *See* Office Action at page 13. As stated in the reply to the previous Office Action (the reply mailed June 29, 2005), and contrary to the Examiner's position, the specification provides ample guidance in how to prevent an acute episode of asthma.

The Examiner applied the Wands factors to the analysis of the claims in view of the enablement requirement. Accordingly, and with respect to the guidance provided in the specification, the Examiner stated that "[a]ll of the guidance provided by the specification is directed towards treatment rather than prevention of an acute episode of asthma." *See* Office Action at page 4. This is simply not true. The specification at page 3, lines 18-19, states "We contemplate preventive use when the patient expects to encounter asthma inducing conditions e.g. intends to take exercise or go into smoky conditions." Further, a method of prevention or

treatment is described in the specification at page 3, lines 21-27 as including "administering, by inhalation,...an effective amount of a composition comprising, in admixture: (a) a first active ingredient which is formoterol, a pharmaceutically acceptable salt or solvate thereof or a solvate of such a salt; and (b) a second active ingredient which is budesonide."

With respect to working examples, the Examiner stated that "[a]ll of the working examples are directed toward the treatment rather than prevention of an acute episode of asthma." *See* Office Action at page 4. The Examiner, however, is reminded that working examples are not required to enable a claim. As stated by the U.S. Court of Customs and Patent Appeals, "The mere fact that something has not been previously done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it." *In re Chilowsky*, 229 F.2d 457, 461 (CCPA 1956). Furthermore, "a specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation." *In re Borkowski*, 422 F.2d 904 (CCPA 1970). Indeed, undue experimentation is not required to practice the claimed methods. As explained in the reply mailed June 29, 2005, a patient will know ahead of time when he is likely to experience asthma symptoms. For example, a patient will know ahead of time when he plans to exercise, and can predict that he may experience asthma symptoms when he exercises. Since the patient will know that he may experience asthma symptoms when he exercises, he will know when to take the preventative dose of the claimed composition (*i.e.*, before he exercises).

Regarding the amount of experimentation necessary to practice the claimed methods, the Examiner stated that "one of skill in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration..." *See* Office Action at page 5. However, Applicant asserts that there is little to "envision" because these parameters are described sufficiently in the specification to enable the claimed methods. For example, pharmaceutically acceptable additives, diluents and carriers in suitable amounts are described in the specification, *e.g.*, at page 6, lines 6-10. Appropriate dosages of formoterol and budesonide are described, *e.g.*, at page 5, lines 19-30. Duration of treatment is described, *e.g.*, at page 4, line 5 ("as often as needed") and line 22 ("on an as needed basis"). Routes of administration are described, *e.g.*, at page 6, lines 19-21. The Examiner has

not provided any explanation why the guidance provided in the specification is not sufficient to enable the claimed methods for prevention of asthma symptoms.

Further, Applicant reiterates the point made in the reply mailed June 29, 2005 (the "June 29th reply"), that a realistic, art-recognized definition of "prevent" should be applied to the claims. As explained previously, anti-inflammatory agents such as budesonide have long been used as "maintenance" drugs to control symptoms and reduce the number of exacerbations experienced by the patient, regardless of the underlying triggering cause. In other words, anti-inflammatory agents are used *inter alia* to prevent symptoms, including exacerbations, experienced by the asthmatic patient. Exhibit A (the product insert from the Pulmicort Turbuhaler budesonide inhalation powder inhaler) submitted with the June 29th reply even explains at page 2 that "Pulmicort Turbuhaler works to prevent and reduce your asthma symptoms and attacks." The various internet publications submitted as Exhibit F in the June 29th reply also demonstrated the general understanding that budesonide inhalation can be used to prevent asthma attacks. In view of this extrinsic evidence, there is, again, no reason to expect that undue experimentation would be required to practice the claimed methods. In an effort to clarify the meaning of the claims, the preambles of independent claims 13, 35, 36, and 42 have been amended to recite the "prevention and treatment of asthma symptoms." Applicant requests that the Examiner reconsider the evidence submitted with the previous reply in view of the amendments to the claims.

In view of the guidance provided in the specification and the exhibits submitted with the June 29th reply, undue experimentation is not required to practice the claimed methods. Applicant therefore maintains that the claims are enabled and respectfully requests that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

35 U.S.C. § 103(a)

The Examiner maintained the rejection of claims 13-15, 17, 18, 20-36, 38, and 42, and further rejected claim 43, as being unpatentable over Carling *et al.* of record. The Examiner stated that "to instruct the patient to inhale, on demand, as determined by the patient's symptoms in acute asthmatic episode is obvious since Carling *et al.* teach that the dosages strongly depends on the severity of disease...and the suitable daily dosage is up to 8 inhalations." *See* Office

Action at page 7. In response to the exhibits and arguments submitted by the Applicant in the June 29th reply, the Examiner stated, *inter alia,* that

> Applicant essentially argues Exhibits teach each and every one of the doses to be administered as 'twice daily' and there is no provision for additional doses to be taken 'as needed' and regardless of whether the patient is feeling better or worse on a given day the patients would not to take more or less than the exact dose prescribed by the physician. This is not persuasive because Carling et al. teach by the examples on pages 7-9 the amounts of the active agents in combination to be used per day. The maximum dosage amounts taught by Carling et al. allows up to 8 daily inhalations of the combination (budesonide/formoterol) to the asthmatic patients. *See* Office Action at page 10.

Applicant maintains that Carling *et al.* teaches administration of the formoterol/budesonide combination at a maximum of two doses per day, not the maximum 8 daily inhalations as asserted by the Examiner. At page 4, lines 19-21, Carling *et al.* discloses that "the combination according to the present invention permits a twice daily dosing regime..." Furthermore, the third full paragraph at page 6 of Carling begins with the statement: "The intended dose regimen is a twice daily administration." The varying dosage discussed by Carling in the remainder of that paragraph was meant to convey that different patients may be prescribed different daily doses that will depend on such factors as the particular patient's age and weight, and the severity of that particular patient's disease as determined by the physician. *Any given patient is prescribed a fixed daily dose.* Regardless of the fixed daily dose prescribed for a given patient, that patient will be instructed to take the entire prescribed daily dose (no more and no less), split into just two administrations per day. Exhibits A-E presented in the June 29th reply support the interpretation of Carling as intending a maximum of only two administrations per day. There is no suggestion or motivation in Carling *et al.* to inhale the combination more than twice per day, as needed or "on demand" as required by the claimed methods.

The Examiner stated that "the molar ratio of active agents to be used set forth in claim 14, the selection of carrier set forth in claims 23 and 24, and the particle size of active agents set forth in claim 22, are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional formulations." *See* Office Action at page 8.

Claims 14 and 22-24 depend from claim 13, and are therefore patentable for at least the reasons discussed above.

Claims 16 and 19 were rejected as being unpatentable over Carling *et al.* in view of Aberg *et al.* and Ryrfeldt *et al.* of record. The Office Action states at page 9 that "Carling *et al.* do teach the isomer of formoterol set forth in claim 16 and the specified epimer of budesonide set forth in claim 19." Applicant finds no such teaching in Carling *et al.*, and asks the Examiner to point it out. The Examiner also stated that

> it would have been obvious to one of ordinary skill in the art to employ (R,R) enantiomer of formoterol and 22R epimer of budesonide in view of Aberg *et al.* and Ryrfeldt *et al.* because both of the references of Aberg and Ryrfeldt teach specific isomers form that possesses potent asthmatic effect of the active agents utilized in Carling reduced adverse effects in treatment of asthma. One would have been motivated to employ (R,R) isomer of formoterol and 22R epimer of budesonide in Carling's composition with reasonable expectation of successfully treating asthmatic patients with reduced adverse effects. *See* Office Action at page 9.

Applicant maintains that claims 16 and 19, which depend from claim 13, are patentable for at least the reasons discussed above. The teachings of Aberg *et al.* and Ryrfeldt *et al.* do not make up for Carling's deficiencies as outlined above, and indeed are cited solely for their teachings concerning specific epimers of the active ingredients.

In view of the foregoing, Applicant requests reconsideration and withdrawal of the rejection of claims 13-36, 38, 42, and 43 under 35 U.S.C. § 103(a).

No fees are believed to be due. If this is incorrect, please apply any necessary charges or any credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 06275-188001.

Respectfully submitted,

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